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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/781,076	02/08/2001	Benjamin Oshlack	200.1134	7481

7590 03/27/2003

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EXAMINER
RUSSEL, JEFFREY E

ART UNIT	PAPER NUMBER
1654	

DATE MAILED: 03/27/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/781,076	OSHLACK ET AL.	
	Examiner	Art Unit	
	Jeffrey E. Russel	1654	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 January 2003* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *37 and 40-49* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *37 and 40-49* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

1. Applicants are requested to check the spelling of "cyclazacine" at claim 37, line 8. The Merck Index, 13th edition, gives the spelling as "cyclazocine".

2. The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

3. Claims 37 and 40-47 are rejected under 35 U.S.C. 103(a) as being obvious over Crain et al (U.S. Patent No. 5,767,125) in view of Reder et al (U.S. Patent No. 5,968,547). Crain et al teach co-administration of an opioid agonist and an opioid antagonist where the opioid antagonist is in an amount sufficient to attenuate the anti-analgesia, hyperalgesia, hyperexcitability, physical dependence, and/or tolerance effects of the opioid agonist. The opioid agonist can be fentanyl, buprenorphine, or morphine. The opioid antagonist can be naloxone or naltrexone. The opioid agonist and opioid antagonist can be administered transdermally, such as with a patch. See, e.g., column 4, lines 35-42 and 60-67; column 5, lines 9-14; column 5, line 60 - column 6, line 6; and column 6, lines 20-25. Crain et al do not teach an opioid agonist which is hydromorphone, oxycodone, or salts thereof. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to use hydromorphone, oxycodone, or salts thereof as the opioid agonists required by Crain et al because Crain et al are not limited to any particular opioid agonists, because hydromorphone, oxycodone, and salts thereof are known opioid agonists, and because substitution of a known species for a genus in order to obtain the benefits expected for the known species is prima facie obvious. Crain et al are not limited to any particular transdermal delivery system, but do not teach one with a delivery time of at least 3 days. Reder et al teach administration of an opioid agonist using a transdermal delivery system which releases the agonist over a period of 5 days.

See, e.g., the abstract and claim 1. It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to administer the analgesic combination of Crain et al using the transdermal delivery system of Reder et al because Crain et al's analgesic combination can be administered using any transdermal delivery system, because Reder et al's transdermal system is used to deliver analogous compounds for the same analgesic purpose, and because use of Reder et al's transdermal system will permit long-time pain relief with minimal intrusion to the patient.

4. Claims 48 and 49 are rejected under 35 U.S.C. 103(a) as being obvious over Crain et al (U.S. Patent No. 5,767,125) in view of Reder et al (U.S. Patent No. 5,968,547) as applied against claims 37 and 40-47 above, and further in view of the WO Patent Application 00/01377 or Simon (U.S. Patent No. 6,103,258). Crain et al and Reder et al do not teach releasing the opioid agonist and antagonist at substantially proportionate rates. The WO Patent Application '377 teaches co-administration of opioid agonists and antagonists by intramuscular, intravenous, nasal, oral, sublingual or transdermal methods, recognizes that the individual components can have different pharmacokinetic profiles and different in vivo life spans, and teaches providing a controlled release matrix or coating to the shorter-acting component so that its pharmacokinetic profile better matches the profile of the longer-acting component, i.e. so that their release rates are proportional. See, e.g., page 17, line 22 - page 18, line 26; page 22, lines 20-22; and page 22, line 30 - page 23, line 8. Simon is the U.S. equivalent of the WO Patent Application 00/01377 and contains the same disclosure as that of the WO Patent Application '377 (see, e.g., column 9, line 39 - column 10, line 18, and column 12, lines 33-60). It would have been obvious to one of ordinary skill in the art at the time Applicants' invention was made to provide controlled release

matrices or coatings as taught by the WO Patent Application '377 and Simon to the agonist or antagonist of Crain et al as modified above by Reder et al so that the problem of different pharmacokinetic profiles and in vivo lifespans is avoided.

5. Applicant's arguments filed January 29, 2003 have been fully considered but they are not persuasive.

The examiner agrees with Applicants' argument as to why the WO Patent Application 00/01377 does not teach or suggest transdermal administration of combinations of naloxone or naltrexone with opioid agonists. Further, the prior art of record does not teach or suggest that cyclazacine or levallorphan are kappa opioid antagonists equivalent to nalmefene such that there would be motivation to use cyclazacine or levallorphan as the kappa opioid antagonists required by the WO Patent Application '377. However, these distinctions over the WO Patent Application '377 do not apply to Crain et al as applied above, which suggests the transdermal administration of the combinations of opioid agonists and opioid antagonists recited in Applicants' claims.

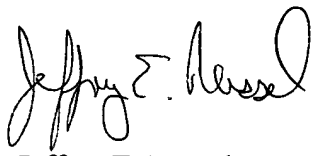
6. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37

CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jeffrey E. Russel at telephone number (703) 308-3975. The examiner can normally be reached on Monday-Thursday from 8:30 A.M. to 6:00 P.M. The examiner can also be reached on alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor Brenda Brumback can be reached at (703) 306-3220. The fax number for Art Unit 1654 for formal communications is (703) 305-3014; for informal communications such as proposed amendments, the fax number (703) 746-5175 can be used. The telephone number for the Technology Center 1 receptionist is (703) 308-0196.



Jeffrey E. Russel

Primary Patent Examiner

Art Unit 1654

JRussel

March 26, 2003